


 Rec'd PCT/PTO 12 JUN 2002 *FS*

SEQUENCE LISTING

<110> Merck Frosst Canada & Co.

 <120> USE OF GABAPENTIN IN ASSAYS TO IDENTIFY
 GABAB RECEPTOR AGONISTS, INVERSE AGONISTS, ANTAGONISTS, AND
 ALLOSTERIC MODULATORS OF AGONISTS

<130> 20395 PCT

<140> PCT/CA00/00638

<141> 2000-05-30

<150> 60/137,025

<151> 1999-06-01

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Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys Val
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Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val Phe
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Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp Phe
115 120 125
Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile Cys
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Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn Arg
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Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro
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Glu	Leu	Lys	Leu	Ile	His	His	Asp	Ser	Lys	Cys	Asp	Pro	Gly	Gln	Ala
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Thr	Lys	Tyr	Leu	Tyr	Glu	Leu	Leu	Tyr	Asn	Asp	Pro	Ile	Lys	Ile	Ile
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Leu	Met	Pro	Gly	Cys	Ser	Ser	Val	Ser	Thr	Leu	Val	Ala	Glu	Ala	Ala
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Arg	Met	Trp	Asn	Leu	Ile	Val	Leu	Ser	Tyr	Gly	Ser	Ser	Ser	Pro	Ala
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Leu	Ser	Asn	Arg	Gln	Arg	Phe	Pro	Thr	Phe	Phe	Arg	Thr	His	Pro	Ser
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Trp	Lys	Lys	Ile	Ala	Thr	Ile	Gln	Gln	Thr	Thr	Glu	Val	Phe	Thr	Ser
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Thr	Leu	Asp	Asp	Leu	Glu	Glu	Arg	Val	Lys	Glu	Ala	Gly	Ile	Glu	Ile
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Thr	Phe	Arg	Gln	Ser	Phe	Phe	Ser	Asp	Pro	Ala	Val	Pro	Val	Lys	Asn
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Glu	Ala	Arg	Lys	Val	Phe	Cys	Glu	Val	Tyr	Lys	Glu	Arg	Leu	Phe	Gly
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Lys	Lys	Tyr	Val	Trp	Phe	Leu	Ile	Gly	Trp	Tyr	Ala	Asp	Asn	Trp	Phe
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Lys	Thr	Tyr	Asp	Pro	Ser	Ile	Asn	Cys	Thr	Val	Glu	Glu	Met	Thr	Glu
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Ala	Val	Val	Phe	Pro	Leu	Gly	Leu	Asp	Gly	Tyr	His	Ile	Gly	Arg	Ser
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Gln	Phe	Pro	Phe	Val	Cys	Gln	Ala	Arg	Leu	Trp	Leu	Leu	Gly	Leu	Gly
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Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp
705          710          715
Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr
    725          730          735
Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser
    740          745          750
Ile Leu Pro Gln Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp
    755          760          765
Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile
770          775          780
Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp
785          790          795
His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu
    805          810          815
Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala
    820          825          830
Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu
    835          840          845
Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu
    850          855          860
Trp Gln Ser Glu Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn
865          870          875
Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu
    885          890          895
Leu Glu Lys Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg
    900          905          910
His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro
    915          920          925
Thr Pro Pro Asp Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro
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Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys
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<211> 962
<212> PRT
<213> Homo Sapiens

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Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
    35          40          45
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
    50          55          60
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
65          70          75          80
Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
    85          90          95
Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
    100          105          110
Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Ala Asp
    115          120          125
Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Arg Ser Ile
    130          135          140
Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn

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Ala	Arg	Met	Trp	Asn	Leu	Ile	Val	Leu	Ser	Tyr	Gly	Ser	Ser	Ser	Pro	
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Ala	Leu	Ser	Asn	Arg	Gln	Arg	Phe	Pro	Thr	Phe	Phe	Arg	Thr	His	Pro	
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Ile	Thr	Phe	Arg	Gln	Ser	Phe	Phe	Ser	Asp	Pro	Ala	Val	Pro	Val	Lys	
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Asn	Leu	Lys	Arg	Gln	Asp	Ala	Arg	Ile	Ile	Val	Gly	Leu	Phe	Tyr	Glu	
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Thr	Glu	Ala	Arg	Lys	Val	Phe	Cys	Glu	Val	Tyr	Lys	Glu	Arg	Leu	Phe	
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Gly	Lys	Lys	Tyr	Val	Trp	Phe	Leu	Ile	Gly	Trp	Tyr	Ala	Asp	Asn	Trp	
385					390					395					400	
Phe	Lys	Ile	Tyr	Asp	Pro	Ser	Ile	Asn	Cys	Thr	Val	Asp	Glu	Met	Thr	
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Ala	Asn	Thr	Arg	Ser	Ile	Ser	Asn	Met	Thr	Ser	Gln	Glu	Phe	Val	Glu	
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Lys	Leu	Thr	Lys	Arg	Leu	Lys	Arg	His	Pro	Glu	Glu	Thr	Gly	Gly	Phe	
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Gln	Glu	Ala	Pro	Leu	Ala	Tyr	Asp	Ala	Ile	Trp	Ala	Leu	Ala	Leu	Ala	
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Cys	Leu	Ser	Phe	Asn	Ile	Tyr	Asn	Ser	His	Val	Arg	Tyr	Ile	Gln	Asn	
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625					630					635				640		
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Asn	Gln	Phe	Pro	645	Phe	Val	Cys	Gln	Ala	Arg	Leu	Trp	Leu	Leu	655	Gly	Leu
Gly	Phe	Ser	660	Leu	Gly	Tyr	Gly	Ser	665	Met	Phe	Thr	Lys	Ile	670	Trp	Val
His	Thr	675	Val	Phe	Thr	Lys	Lys	Glu	680	Glu	Lys	Lys	Glu	685	Trp	Arg	Lys
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Asp	Val	705	Leu	Thr	Leu	Ala	Ile	Trp	710	Gln	Ile	Val	Asp	715	Pro	Leu	His
Thr	Ile	720	Glu	Thr	Phe	Ala	Lys	Glu	725	Glu	Pro	Lys	Glu	730	Asp	Ile	Asp
Ser	Ile	735	Leu	Pro	Gln	Leu	Glu	His	740	Cys	Ser	Ser	Arg	745	Lys	Met	Asn
Trp	Leu	750	Gly	Ile	Phe	Tyr	Gly	Tyr	755	Lys	Gly	Leu	Leu	760	Leu	Leu	Gly
Ile	Phe	765	Leu	Ala	Tyr	Glu	Thr	Lys	770	Ser	Val	Ser	Thr	775	Glu	Lys	Ile
Asp	His	780	Arg	Ala	Val	Gly	Met	Ala	785	Ile	Tyr	Asn	Val	790	Ala	Val	Leu
Leu	Ile	800	Thr	Ala	Pro	Val	Thr	Met	805	Ile	Leu	Ser	Ser	810	Gln	Gln	Asp
Ala	Phe	815	Ala	Phe	Ala	Ser	Leu	Ala	820	Ile	Val	Phe	Ser	825	Tyr	Ile	Thr
Leu	Val	830	Val	Leu	Phe	Val	Pro	Lys	835	Met	Ile	Arg	Arg	840	Leu	Ile	Thr
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Thr	Asn	860	Asn	Asn	Glu	Glu	Glu	Lys	865	Arg	Leu	Leu	Glu	870	Lys	Glu	Asn
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Pro	Pro	910	Thr	Pro	Pro	Glu	Pro	Ser	915	Gly	Gly	Leu	Pro	920	Arg	Gly	Pro
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<210> 25

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Homo Sapiens

<400> 25

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<210> 26

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Homo Sapiens

<400> 26

Asp	Tyr	Lys	Asp	Asp	Asp	Asp	Lys
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<210> 27

<211> 753

<212> PRT

<213> Caenorhabditis Elegans

<400> 27

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			20					25					30		
Glu	Ser	Gly	Ser	Gly	Gly	Trp	Ala	Gly	Gly	Glu	Ala	Cys	Leu	Pro	Ala
		35					40					45			
Val	Glu	Met	Ala	Leu	Lys	Asp	Val	Asn	Ser	Arg	Leu	Asp	Ile	Leu	Pro
	50					55					60				
Gly	Tyr	Val	Leu	Asn	Met	Thr	Asn	His	Asn	Ser	Gln	Cys	Gln	Pro	Gly
65					70					75				80	
Leu	Ala	Met	Gln	Gln	Leu	Tyr	Asp	Phe	Leu	Tyr	Lys	Pro	Pro	Thr	Lys
				85					90					95	
Leu	Met	Leu	Leu	Thr	Gly	Cys	Ser	Pro	Val	Thr	Thr	Val	Ile	Ala	Glu
			100					105					110		
Ala	Ala	Pro	Val	Trp	Lys	Leu	Val	Val	Leu	Ser	Tyr	Gly	Gly	Ser	Ser
		115				120						125			
Pro	Ala	Leu	Ser	Asn	Arg	Asn	Arg	Phe	Pro	Thr	Leu	Phe	Arg	Thr	His
		130				135					140				
Pro	Ser	Ala	Asn	Met	Gln	Asn	Pro	Thr	Arg	Ile	His	Ile	Met	Glu	Lys
145					150					155				160	
Phe	Lys	Trp	Lys	Arg	Phe	Thr	Ile	Leu	Met	Ser	Val	Glu	Glu	Val	Phe
				165					170					175	
Val	Thr	Thr	Ala	Lys	Asp	Leu	Glu	Val	Ser	Glu	Arg	Lys	Lys	Gly	Ile
			180					185					190		
Lys	Val	Asp	Arg	Gln	Ser	Phe	Tyr	Gly	Asp	Pro	Thr	Asp	Ala	Met	Lys
		195					200					205			
Thr	Leu	Gln	Arg	Gln	Asp	Ala	Arg	Ile	Ile	Val	Gly	Leu	Phe	Tyr	Val
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Thr	Glu	Ala	Arg	Lys	Val	Leu	Cys	Gln	Ala	Tyr	His	His	Gly	Leu	Tyr
225					230					235				240	
Gly	Arg	Arg	Tyr	Val	Trp	Phe	Phe	Ile	Gly	Trp	Tyr	Ala	Asp	Thr	Trp
				245					250					255	
Tyr	Ile	Pro	Pro	Pro	Glu	Glu	His	Leu	Asn	Cys	Thr	Ala	Glu	Gln	Met
			260					265					270		
Thr	Glu	Ala	Ala	Glu	Tyr	His	Phe	Thr	Thr	Glu	Ser	Val	Met	Leu	Ser
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Arg	Asp	Asn	Ile	Pro	Ala	Ile	Ser	Glu	Met	Thr	Gly	Met	Gln	Phe	Gln

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Gln	Arg	Leu	Thr	Gln	Tyr	Phe	Gln	Lys	Asp	Thr	Ala	Asn	Val	Gly	Gly	
305					310					315					320	
Phe	Pro	Glu	Ala	Pro	Leu	Ala	Tyr	Asp	Ala	Val	Trp	Ala	Leu	Ala	Leu	
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Ala	Phe	Asn	Cys	Thr	Arg	Asn	Asn	Leu	Pro	Ser	His	Ile	Arg	Leu	Glu	
			340					345					350			
Asn	Phe	Thr	Tyr	Asp	Asn	Lys	Val	Ile	Ala	Asp	Thr	Leu	Phe	Gln	Cys	
		355					360					365				
Val	Lys	Asn	Thr	Ser	Phe	Arg	Gly	Val	Ser	Gly	Lys	Val	Met	Phe	Ser	
	370					375					380					
Asp	Ser	Gly	Asp	Arg	Ile	Ala	Arg	Thr	Gln	Ile	Glu	Gln	Met	Gln	Gly	
385				390					395						400	
Gly	Lys	Tyr	Lys	Ile	Met	Gly	Tyr	Tyr	Asp	Thr	Thr	Ser	Gly	Asp	Leu	
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Glu	Trp	Tyr	Asn	Lys	Glu	Gln	Trp	Leu	Asn	Gly	Lys	Gly	Pro	Pro	Pro	
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Asp	Ser	Thr	Val	Ile	Lys	Thr	Phe	Asn	Ser	Tyr	Ser	Asp	Phe	Leu	Ile	
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Phe	Ser	Ser	Thr	Ile	Leu	Gln	Tyr	Phe	Ser	Gln	Phe	Leu	Ala	Leu	Leu	
	450					455					460					
His	Val	Ser	Ser	Phe	Thr	Phe	Leu	His	Lys	Asn	Ile	Ile	Phe	Gln	Ser	
465				470						475					480	
Gln	Pro	Glu	Cys	Asn	Asn	Ile	Leu	Leu	Ile	Gly	Cys	Ser	Leu	Cys	Leu	
				485					490					495		
Phe	Ser	Leu	Phe	Leu	Ile	Gly	Leu	Pro	Ser	Asp	Asp	Ile	Ser	Ile	Ser	
			500					505					510			
Glu	Ser	Leu	Phe	Pro	Leu	Leu	Cys	His	Ala	Arg	Val	Thr	Ile	Leu	Leu	
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Phe	Gly	Phe	Thr	Phe	Ala	Tyr	Gly	Ser	Met	Phe	Ala	Lys	Val	Trp	Ile	
	530					535					540					
Val	His	Arg	Met	Gly	Ala	Thr	Glu	Asn	Gln	Gln	Leu	Ala	Ser	Arg	Gln	
545				550					555						560	
Pro	Ile	Ser	Ser	Ser	Lys	Phe	Tyr	Val	Ile	Val	Ala	Ala	Leu	Thr	Ala	
				565					570					575		
Val	Asp	Val	Phe	Val	Cys	Phe	Val	Trp	Val	Leu	Ile	Asp	Pro	Leu	His	
			580					585					590			
Leu	Thr	Glu	Gln	Lys	Phe	Pro	Leu	Phe	Ala	Asp	Ser	Glu	Glu	Asp	Glu	
		595					600					605				
Met	Ile	Met	Pro	Val	Leu	Gln	Gln	Cys	Gln	Ser	Asn	Gln	Gln	Glu	Val	
	610					615						620				
Trp	Ile	Gly	Ile	Ile	Met	Gly	Phe	Lys	Cys	Leu	Leu	Val	Phe	Gly		
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Thr	Phe	Leu	Ser	Tyr	Glu	Thr	Arg	Asn	Leu	Lys	Leu	Arg	Phe	Ile	Asn	
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Asp	Ser	Arg	Phe	Val	Gly	Leu	Ala	Ile	Tyr	Asn	Val	Ala	Val	Met	Thr	
			660					665					670			
Leu	Val	Thr	Ala	Pro	Val	Val	Thr	Leu	Ile	His	Gly	Lys	Val	Asp		
		675					680					685				
Ala	Asn	Phe	Ala	Phe	Ile	Ser	Leu	Thr	Ser	Val	Leu	Ile	Cys	Thr	Tyr	
	690					695					700					
Ile	Ser	Val	Gly	Leu	Ile	Tyr	Gly	Pro	Lys	Ile	Arg	His	Ile	Ile	Lys	
705					710					715					720	
Val	Pro	Pro	Ser	Ala	Asp	Glu	Ile	Gln	Leu	Asn	Gly	Asn	Val	Gly	Pro	
				725					730					735		
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<210> 28
 <211> 659

<212> PRT

<213> Caenorhabditis Elegans

<400> 28

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Thr	Ala	Leu 35	Ser	His	Val	His	Ser 40	Arg	Ser	Cys	Ile	Leu 45	Gln	Gly	Tyr
Arg	Leu 50	Glu	Met	Ile	Val	Lys 55	Asp	Thr	His	Cys	Lys 60	Thr	Ser	Gln	Gly
Met 65	Lys	Ala	Leu	Phe	Asp 70	Leu	Ile	Ala	Ser	Arg 75	Pro	Arg	Pro	Val	Ala 80
Ile	Leu	Gly	Gly	Gln 85	Cys	Thr	Glu	Val	Asn 90	Glu	Pro	Ile	Ala 95	Met	Ala
Leu	Lys	Tyr	Trp 100	Gln	Ile	Val	Gln	Leu 105	Ser	Tyr	Ala	Glu	Thr 110	His	Ala
Met	Asn	Gly 115	Gln	Leu	Gln	Leu	Phe 120	Thr	Thr	Phe	Phe	Arg 125	Val	Val	Pro
Gly	Ser 130	Arg	Asn	Thr	Asn	Met 135	Ala	Lys	Cys	Lys	Phe 140	Val	Asn	His	Phe
Gly 145	Trp	Lys	Arg	Val	Gly 150	Thr	Val	Lys	Gln	Asn 155	Asp	Gln	Pro	Arg	Tyr 160
Ala	Leu	Val	Arg	Asp 165	Val	Arg	Ile	Ile	Leu 170	Val	Asp	Val	Asp	Glu 175	Glu
Met	Ala	Ala	Thr 180	Val	Leu	Cys	Ala	Gly 185	Tyr	His	Arg	Gly	Met 190	Tyr	Gly
Asp	Asn	Tyr 195	Val	Trp	Ile	Leu	Pro 200	Gly	Tyr	His	Ser	Asp 205	Arg	Trp	Leu
Asn	Gln 210	Thr	His	Asp	Asn	Cys 215	Thr	Val	Glu	Glu	Met 220	Arg	Glu	Ala	Ala
Lys 225	Asn	His	Phe	Ser	Val 230	Glu	Phe	Ala	Leu	Thr 235	Arg	Arg	Asp	Val	Asp 240
Thr	Lys	Ile	Val	Gly 245	Asn	Thr	Val	Ser	Pro 250	Tyr	Val	Thr	Leu	Asn 255	Leu
Phe	Gln	Arg	Ala 260	Gly	Asp	Val	Trp	Asn 265	Glu	Ile	Thr	Gln	Leu 270	Asp	Pro
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Ile	Ala 290	Leu	Ser	His	Ser	Met 295	Gly	Asp	Asn	Ala	Glu 300	Phe	Ser	His	His
Lys 305	Met	Met	Glu	Ala	Ile 310	Asp	Asn	Ser	Ser	Phe 315	Gln	Gly	Leu	Thr	Gly 320
Lys	Val	Lys	Phe	Ala 325	Asn	Asn	Glu	Arg	Leu 330	Gly	Leu	Val	Asp	Ile 335	Lys
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Pro	Leu 370	Asp	Ser	Thr	Ile	Thr 375	Glu	Arg	Arg	Arg	Glu 380	His	Ile	Ser	Ser
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Val	Ser 450	Pro	Asp	Val	Phe	Val 455	Trp	Leu	Cys	Tyr	Thr 460	Lys	Thr	Trp	Thr

Leu	Cys	Ile	Gly	Phe	Thr	Leu	Ser	Phe	Gly	Ala	Met	Phe	Ser	Lys	Thr
465					470					475					480
Trp	Arg	Val	His	Ser	Ile	Phe	Thr	Asn	Ile	Arg	Met	Asp	Arg	Lys	Ala
				485					490					495	
Ile	Lys	Asp	Ser	Lys	Leu	Phe	Ile	Ile	Leu	Gly	Ile	Leu	Leu	Phe	Ile
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Thr	Val	Glu	Gln	Phe	Lys	Phe	Leu	Ile	Phe	Ser	Ala	Arg	Arg	Asn	Ile
	530					535					540				
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Phe	Gln	Ala	Val	Leu	Tyr	Ala	Val	Lys	Gly	Val	Leu	Met	Ile	Leu	Gly
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Cys	Phe	Leu	Ala	Trp	Glu	Thr	Arg	His	Val	Asn	Val	Pro	Ala	Leu	Asn
			580					585					590		
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		595					600					605			
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Leu	Cys	Leu	Val	Phe	Val	Pro	Lys	Val	Arg	Phe	Leu	Glu	Leu	Cys	Cys
				645					650					655	
Ile	Gly	Ser													